PROVIDER POLICIES & PROCEDURES

GENE-BASED THERAPY FOR DUCHENNE MUSCULAR DYSTROPHY (DMD)

The primary purpose of this document is to assist providers enrolled in the Connecticut Medical Assistance Program (CMAP) with the information needed to support a medical necessity determination for gene-based therapy for Duchenne muscular dystrophy (DMD). By clarifying the information needed for prior authorization of services, HUSKY Health hopes to facilitate timely review of requests so that individuals obtain the medically necessary care they need as quickly as possible.

This policy applies to the following gene-based therapies for DMD: Exondys 51 (eteplirsen), Vyondys 53 (golodirsen), Viltepso (viltolarsen), Amondys 45 (casimersen) and Elevidys (delandistrogene moxeparvovec-rokl).

Exon-Skipping Gene Therapies:

- Exondys 51 (eteplirsen) is a prescription medication used to treat DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping.
- Vyondys 53 (golodirsen) and Viltepso (viltolarsen) are prescription medications used to treat DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping.
- Amondys 45 (casimersen) is a prescription medication used to treat DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 45 skipping.

Micro-dystrophin Gene Therapies:

- Elevidys (delandistrogene moxeparvovec-rokl) is a one-time infused adeno-associated virus vector-based gene therapy used to treat DMD in ambulatory pediatric patients aged 4 through 5 years who have a confirmed mutation of the DMD gene. It leads to the production of Elevidys micro-dystrophin that contains selected domains of the dystrophin protein present in normal muscle cells.

CLINICAL GUIDELINE

Coverage guidelines for gene-based therapy for DMD will be made in accordance with the DSS definition of Medical Necessity. The following criteria are guidelines *only*. Coverage guidelines are based on an assessment of the individual and their unique clinical needs. If the guidelines conflict with the definition of Medical Necessity, the definition of Medical Necessity shall prevail. The guidelines are as follows:

A. Exon-Skipping Gene Therapies (Exondys 51, Vyondys 53, Viltepso, Amondys 45)

1. **Initial Authorization**
   An initial 6-month trial of gene-based exon-skipping therapy for DMD may be considered medically necessary when the following criteria are met:

   a. The individual has a diagnosis of DMD and a mutation amenable to exon 51 skipping (Exondys 51), exon 53 skipping (Vyondys 53 and Viltepso), or exon 45 skipping

(Amondys 45) confirmed by genetic testing (ordering physician MUST provide results of genetic testing); **AND**

b. Therapy must be prescribed by or in consultation with a physician who specializes in the treatment of DMD; **AND**
c. The individual is currently receiving treatment with corticosteroids unless contraindicated or unable to tolerate; **AND**
d. Baseline age-appropriate motor function and pulmonary function tests have been performed; **AND**
e. The physician will follow all FDA recommendations for dosing, administration, and monitoring.

2. **Reauthorization**
   Continuation of treatment with exon-skipping therapies may be considered medically necessary at 6-month intervals if the individual is continuing to benefit from therapy. A signed letter from the individual's ordering physician is required documenting a positive clinical response.

Note: There is currently no established efficacy for concomitant therapy with two or more DMD gene-based exon-skipping therapies. Requests for treatment with more than one agent will be reviewed on a case-by-case basis.

B. Micro-dystrophin Gene Therapies (Elevidys)

1. **Initial Authorization**
   Gene-based micro-dystrophin therapy Elevidys (delandistrogene moxeparvovec-rokl) for DMD may be considered medically necessary when the following criteria are met:

   a. The individual has a diagnosis of DMD with a mutation in the DMD gene confirmed by genetic testing (ordering physician MUST provide results of genetic testing); **AND**
   b. The individual does not have a deletion in exon 8 and/or exon 9 in the DMD gene; **AND**
   c. The individual is 4 through 5 years of age when treatment will be administered; **AND**
   d. The individual is ambulatory; **AND**
   e. The individual does not have an elevated anti-AAVrh74 total binding antibody titer ≥ 1:400; **AND**
   f. The individual will receive a corticosteroid regimen prior to and following receipt of Elevidys in accordance with the FDA approved labeling; **AND**
   g. The individual has not received Elevidys in the past; **AND**
   h. Elevidys must be prescribed by or in consultation with a physician who specializes in the treatment of DMD; **AND**
   i. The physician will follow all FDA recommendations for dosing, administration, and monitoring for Elevidys.

2. **Reauthorization**
   Elevidys (delandistrogene moxeparvovec-rokl) is a one-time therapy; more than one administration of Elevidys is considered investigational and not medically necessary.

Investigational and Not Medically Necessary

Any other indication for the use of Exondys 51, Vyondys 53, Viltepso, Amondys 45 and Elevidys is considered investigational and not medically necessary.

NOTE: EPSDT Special Provision
Early and Periodic Screening, Diagnosis, and Treatment (EPSDT) is a federal Medicaid requirement that requires the Connecticut Medical Assistance Program (CMAP) to cover services, products, or procedures for Medicaid enrollees under 21 years of age where the service or good is medically necessary health care to correct or ameliorate a defect, physical or mental illness, or a condition identified through a screening examination. The applicable definition of medical necessity is set forth in Conn. Gen. Stat. Section 17b-259b (2011) [ref. CMAP Provider Bulletin PB 2011-36].

PROCEDURE
Prior authorization is required. Coverage determinations will be based upon a review of requested and/or submitted case-specific information.

The following information is needed to review requests for the above therapies:

1. Fully completed State of Connecticut, Department of Social Services HUSKY Health Program Gene Therapy for DMD Prior Authorization Request form (to include physician's order and signature);
2. Results of genetic testing confirming mutation in the DMD gene (initial authorization requests);
3. Baseline age-appropriate motor function and pulmonary function tests (initial authorization requests);
4. Letter from ordering physician documenting the benefits patient is receiving from treatment (reauthorization requests); and
5. Other information as requested by CHNCT.

Requesting Authorization
Requests must be submitted by the ordering physician and faxed to the number listed on the request form. Questions regarding this form should be directed to the HUSKY Health Program Utilization Management Department at 1.800.440.5071 (select option for medical authorizations).

EFFECTIVE DATE
This Policy for individuals covered under the HUSKY Health Program is effective February 1, 2020.

LIMITATIONS
Not Applicable

CODES:

Code	Definition
J1426	Injection, casimersen, 10mg
J1427	Injection, viltolarsen, 10mg
J1428	Injection, eteplirsen, 10 mg
J1429	Injection, golodirsen, 10mg

Code	Definition
J3590	Unclassified biologics

DEFINITIONS

1. **HUSKY A**: Connecticut children and their parents or a relative caregiver; and pregnant women may qualify for HUSKY A (also known as Medicaid). Income limits apply.
2. **HUSKY B**: Uninsured children under the age of 19 in higher income households may be eligible for HUSKY B (also known as the Children's Health Insurance Program) depending on their family income level. Family cost-sharing may apply.
3. **HUSKY C**: Connecticut residents who are age 65 or older or residents who are ages 18-64 and who are blind, or have another disability, may qualify for Medicaid coverage under HUSKY C (this includes Medicaid for Employees with Disabilities (MED-Connect), if working). Income and asset limits apply.
4. **HUSKY D**: Connecticut residents who are ages 19-64 without dependent children and who: (1) do not qualify for HUSKY A; (2) do not receive Medicare; and (3) are not pregnant, may qualify for HUSKY D (also known as Medicaid for the Lowest-Income populations).
5. **HUSKY Health Program**: The HUSKY A, HUSKY B, HUSKY C, HUSKY D and HUSKY Limited Benefit programs, collectively.
6. **HUSKY Limited Benefit Program or HUSKY, LBP**: Connecticut's implementation of limited health insurance coverage under Medicaid for individuals with tuberculosis or for family planning purposes and such coverage is substantially less than the full Medicaid coverage.
7. **Medically Necessary or Medical Necessity**: (as defined in Connecticut General Statutes § 17b-259b) Those health services required to prevent, identify, diagnose, treat, rehabilitate or ameliorate an individual's medical condition, including mental illness, or its effects, in order to attain or maintain the individual's achievable health and independent functioning provided such services are: (1) Consistent with generally-accepted standards of medical practice that are defined as standards that are based on (A) credible scientific evidence published in peer-reviewed medical literature that is generally recognized by the relevant medical community, (B)recommendations of a physician-specialty society, (C) the views of physicians practicing in relevant clinical areas, and (D) any other relevant factors; (2) clinically appropriate in terms of type, frequency, timing, site, extent and duration and considered effective for the individual's illness, injury or disease; (3) not primarily for the convenience of the individual, the individual's health care provider or other health care providers; (4) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the individual's illness, injury or disease; and (5) based on an assessment of the individual and his or her medical condition.
8. **Prior Authorization**: A process for approving covered services prior to the delivery of the service or initiation of the plan of care based on a determination by CHNCT as to whether the requested service is medically necessary.

ADDITIONAL RESOURCES AND REFERENCES:

1. AMONDYS 45 [Product Information]. Cambridge, Mass. Sarepta Therapeutics, Inc. Revised February 2021. https://amondys45.com/Amondys45_(casimersen)_Prescribing_Information.pdf.
2. A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial for Duchenne Muscular Dystrophy Using SRP-9001. ClinicalTrials.gov identifier: NCT03769116. Updated September 15, 2023. Accessed September 21, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT03769116.
3. A Phase 3 Multinational, Randomized, Double-Blind, Placebo-Controlled Systemic Gene Delivery Study to Evaluate the Safety and Efficacy of SRP-9001 in Subjects With Duchenne Muscular

Dystrophy (EMBARK). ClinicalTrials.gov identifier: NCT05096221. Updated September 8, 2023. Accessed September 21, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT05096221.
4. Anthony K, Feng L, Arechavala-Gomeza V, et al. Exon skipping quantification by quantitative reverse-transcription polymerase chain reaction in Duchenne muscular dystrophy patients treated with the antisense oligomer eteplirsen. *Hum Gene Ther Methods*. 2012;23(5):336-345. doi:10.1089/hgtb.2012.117
5. Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management [published correction appears in Lancet Neurol. 2018 Apr 4;:]. *Lancet Neurol*. 2018;17(3):251-267. doi:10.1016/S1474-4422(18)30024-3
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9. ClinicalTrials.gov. Study of SRP-4045 and SRP-4053 in DMD patients (ESSENCE). Available at: https://clinicaltrials.gov/ct2/show/NCT02500381. Accessed on March 4, 2021.
10. Elevidys [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc.; June 2023
11. Exondys 51 [Product Information]. Cambridge, MA. Sarepta Therapeutics, Inc. Revised July 2020. https://www.exondys51.com/modules/exondys/files/EXONDYS51PI.pdf
12. Frank DE, Mercuri E, Servais, L, et al. Golodirsen induces exon skipping leading to sarcolemmal dystrophin expression in patients with genetic mutations amenable to exon 53 skipping. Poster presented at: Annual Clinical Genetics Meeting of the American College of Medical Genetics and Genomics; April 2-6, 2019; Seattle, WA
13. Institute for Clinical and Economic Review (ICER). Deflazacort, eteplirsen, and golodirsen for Duchenne muscular dystrophy: Effectiveness and value: Evidence Report. July 11, 2019. https://icer-review.org/wpcontent/uploads/2018/12/ICER_DMD_Evidence Report_071119.pdf.
14. Kinane TB, Mayer OH, Duda PW, Lowes LP, Moody SL, Mendell JR. Long-Term Pulmonary Function in Duchenne Muscular Dystrophy: Comparison of Eteplirsen-Treated Patients to Natural History. *J Neuromuscul Dis*. 2018;5(1):47-58. doi:10.3233/JND-170272
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17. Muntoni F, Frank DE, Morgan J, et al. Golodirsen induces exon skipping leading to sarcolemmal dystrophin expression in patients with genetic mutations amenable to exon 53 skipping [abstract]. Neuromuscul Disord. 2018;28:S5. Abstract D01.
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PUBLICATION HISTORY

Status	Date	Action Taken
Original publication	December 2020	Approved at the October 28, 2020 CHNCT Medical Reviewer meeting. Approved by the CHNCT Clinical Quality Subcommittee on December 21, 2020. Approved by DSS on January 7, 2021.
Update	March 2021	Title change. Added coverage guidelines for AMONDYS-45, a new therapy for individuals with DMD that is amenable to exon 45 skipping. Coding update. Changes approved at the March 10, 2021 CHNCT Medical Reviewer meeting. Approved by the CHNCT Clinical Quality Subcommittee on March 15, 2021. Approved by DSS on March 22, 2021.
Update	June 2021	New code C9075 - casimersen, 10mg added. Code effective July 1, 2021. Approved by DSS on July 2, 2021.
Review	June 2022	Reviewed and approved without changes at the June 8, 2022 CHNCT Medical Reviewer meeting. Reviewed and approved without changes by the CHNCT Clinical Quality Subcommittee on June 20, 2022. Approved by DSS on July 5, 2022.
Update	September 2023	Added Elevidys to the policy. Minor formatting and grammatical changes made, and additional references added. Reviewed and approved at the CHNCT Medical Reviewer meeting October 11, 2023. Reviewed and approved by the CHNCT Clinical Quality Subcommittee on December 18, 2023. Approved by DSS on January 03, 2023.